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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/048,024	01/18/2002	Y. Tom Tang	PF-0724 USN	1370

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/048,024	TANG ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7, 9-11, 13, 15-17, 19, 22, 26, 67-69* is/are pending in the application.

4a) Of the above claim(s) *10,13,15,19,22,26,68 and 69* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 9, 11, 16-17, 67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/23/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparison A*.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-7, 9, 11-12, 16-18 drawn to polynucleotide of SEQ ID NO: 5, encoding SEQ ID NO: 1 in the Paper submitted 12/23/2003 is acknowledged. The traversal is on the ground(s) that the Groups drawn to methods of use of the polypeptide could be examined with the products. However, as set forth in the Office Action of 11/19/2003, Where allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP 821.04.

The requirement is still deemed proper and is therefore made FINAL. Claims 10, 13, 15, 19, 22, 26, 68-69 are withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 1-7, 9, 11, 16-17, 67 are under consideration.

Claim Objections

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 66 and 68 have been renumbered as 68 and 69.***Information Disclosure Statement***

The information disclosure statement filed 3/2/2004 fails to comply with 37 CFR 1.52(e), which sets forth the requirements for electronic documents that are to become part of the permanent United States Patent and Trademark Office records in the file of a patent application or reexamination proceeding. Here, the submitted CD does not conform to 37 CFR 1.52(e)(3)(i) which sets forth that each compact disc must conform to the International Standards Organization (ISO) 9660 standard, and the contents of each compact disc must be in compliance with the American Standard Code for Information Interchange (ASCII).

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 9, 11, 16-17, 67 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. Novel biological molecules lack well-established utility and must undergo extensive experimentation.

Specifically, claims 1-7, 9, 11, 16-17, 67 are directed to an isolated polynucleotide comprising the sequence of SEQ ID NO: 5, an expression system comprising the polynucleotide that produces the polypeptide comprising the amino acid sequence of SEQ ID NO: 1, a recombinant host cell, and a process of producing a recombinant host cell and polypeptide, and the polypeptide of SEQ ID NO: 1. The specification alleges that the polypeptides and

polynucleotides are associated with the nervous system. However, the instant specification does not teach any physiologic ligands or functional characteristics of the NSPRT-1 polypeptide and polynucleotide. The specification asserts the following as patentable utilities for the claimed putative NSPRT-1 polynucleotide:

1) to treat certain diseases, including, but not limited to, epilepsy, stroke, Parkinson's disease, kuru, etc.(pg. 33-35)

2) to produce antibodies (pg. 36)

3) in a method of gene therapy (pg. 38)

4)) in screening assays to detect the effects of compounds on the production of mRNA and polypeptide (pg. 43)

5) in diagnosing disease or disease susceptibility associated with the NSPRT-1 gene (pg. 46-50)

Each of these shall be addressed in turn.

1) to treat certain diseases, including, but not limited to, epilepsy, stroke, Parkinson's disease, kuru, etc ...This asserted utility not specific or substantial. The specification does not disclose diseases associated with the NSPRT-1 gene. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease. There is no disclosure, for example, of whether the polynucleotides or polypeptides could be administered orally or parentally, dosages, how to assay for improvement or intolerable levels of side effects, etc. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

2) to produce antibodies (pg. 36). This asserted utility is not substantial or specific. Such methods can be performed with any polypeptide. Further, the specification discloses

nothing specific or substantial for the antibody which is produced by this method. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

3) in a method of gene therapy. This asserted utility not specific or substantial. The specification does not disclose diseases associated with the NSPRT-1 gene. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease. There is no disclosure, for example, of whether the polynucleotides could be administered orally or parentally, dosages, how to assay for improvement or intolerable levels of side effects, etc. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

4) in screening assays to detect the effects of compounds on the production of mRNA and polypeptide. This asserted utility is not specific or substantial. The specification does not disclose disorders associated with the NSPRT-1 gene. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease.

5 in diagnosing disease or disease susceptibility associated with the NSPRT-1 gene. This asserted utility is not specific or substantial. The specification does not disclose disorders associated with the NSPRT-1 gene. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease.

Claims 1-7, 9, 11, 16-17, 67 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Even if, arguendo, a patentable utility if found for the NSPRT-1 polynucleotides or polypeptide, claims 1-7, 9, 11, 16-17, 67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, which would be enabling for a full length NSPRT-1 protein of SEQ ID NO: 1, or a full-length polynucleotide encoding SEQ ID NO: 1, does not reasonably provide enablement for a biologically active fragment of SEQ ID NO: 1, an immunogenic fragment of SEQ ID NO: 1, a naturally-occurring polypeptide at least 90% identical to SEQ ID NO: 1, a polynucleotide sequence 70% identical to SEQ ID NP; 5, or a polynucleotide complementary identical to SEQ ID NO: 5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-7, 9, 11, 16-17, 67 are overly broad since insufficient guidance is provided as to which of the myriad of variant encoded polypeptides which will retain the characteristics of NSPRT-1. The claims are directed to variant polypeptides and polynucleotides encoding variant polypeptides. However, Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of NSPRT-1. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, As an example of the unpredictable effects of mutations on protein function, Mickle et al. teaches that cystic fibrosis is

an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CFTR) (page 597). Several mutations can cause CF, including the G551D mutation. In this mutation a glycine replaces the aspartic acid at position 551, giving rise to the CF phenotype. In the most common CF mutation, delta-F508, a single phenylalanine is deleted at position 508, giving ride to the CF phenotype. Thus showing that even the substitution or deletion of a single amino acid in the entire 1480 amino acid CFTR protein sequence can have dramatic and unpredictable effects on the function of the protein. Additionally, it is known in the art that even a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph). Since the claims encompass variant polypeptides and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The claims do not set forth a functional limitation for the variant polypeptides. The amino acid sequence of a polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because

accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass polynucleotides and encoded polypeptides which the specification only teaches one skilled in the art to test for functional variants. It would require undue experimentation for one of skill in the art to make and use the claimed polypeptides. Since the claims do not enable one of skill in the art to make and use the claimed polypeptides, but only teaches how to screen for the claimed polypeptides, and since detailed information regarding the structural and functional requirements of the polypeptides are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Thus, since Applicant has only taught how to test for polypeptide variants of NSPRT-1, and has not taught how to make polypeptide variants of NSPRT-1, it would require undue experimentation of one of skill in the art to make and use the claimed polypeptides and encoding polynucleotides.

Claims 1-7, 9, 11, 16-17, 67 are rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the

Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims are drawn to a biologically active fragment of SEQ ID NO: 1, an immunogenic fragment of SEQ ID NO: 1, a polynucleotide sequence 70% identical to SEQ ID NP; 5, or a polynucleotide complementary identical to SEQ ID NO: 5, thus these are genus claims. The claims are directed to variant polypeptides and polynucleotides encode variant polypeptides. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claims do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the NSPRT-1 variants. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 5 encoding SEQ ID NO: 1 is insufficient to describe the genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying

characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus of polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides and polypeptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 9, 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7, 9, 16 are vague and indefinite in the recitation of the term "biologically active". The term "biologically active" is not defined by the claim, but give no definition of what this activity is. Various biological activities can be attributed to a peptide. For example, "activity" could constitute transportation throughout a cell, alteration of tertiary structure due to changes in pH, ligand binding, or modulation of second messenger effect, etc. 'Activity' could also be referring to the ability of the fragment to stimulate antibody production.

Claims 1-7, 9, 16 are indefinite in the recitation of the term "naturally occurring". It is unclear whether this term imposes a required limitation on the claim, such that it only encompasses, for example, polypeptides amplified from mRNA isolated from tissue, or only sequences produced by isolation from tissue that contains the polypeptides, or if the claim encompasses all polypeptides. Therefore, the metes and bounds of the claims are unclear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 3, 6, 7, 9, 11, 16 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 98/53059 (Choo et al.).

The Choo reference teaches the amino acid sequences of nucleic acid binding proteins, and the polynucleotides encoding them. The polypeptides of Choo et al. anticipate claim 1 because the claim is drawn to a biologically active fragment of SEQ ID NO: 2, and an immunogenic fragment of SEQ ID NO: 2, while the protein as taught by Choo et a. comprises 7 contiguous amino acids of SEQ ID NO: 2, this meeting the limitations of claims 1 (see Sequence Comparison A, attached). Claims 3, 6 and 7 are anticipated because the Choo reference teaches polynucleotides encoding the polypeptide in a vector (Choo at 13-14 and 21). Claim 9 ius anticipated because the Choo reference teaches a method of producing the polypeptide (Choo at 13, lines 6-16). Claim 11 is anticipated because the polynucleotide encoding the polypeptide in the Choo reference comprises sequence complementary to the polynucleotide of SEQ ID NO: 5. Claim 16 is anticipated because the Choo reference teaches compositions of nucleic acids and pharmaceutical excipients (Choo at 25).

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272-0871.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
March 15, 2004

Sequence Comparison A

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RESULT 16
AAW84306
ID   AAW84306 standard; peptide; 27 AA.
XX
AC   AAW84306;
XX
DT   18-MAR-1999  (first entry)
XX
DE   Finger 3 of a NABP specific for a G12V mutant ras oncogene.
XX
KW   Zinc finger; nucleic acid binding protein; NABP; ras oncogene mutant;
KW   Cys2-His2 zinc finger; detection; gene therapy; gene delivery.
XX
OS   Synthetic.
XX
PN   WO9853059-A1.
XX
PD   26-NOV-1998.
XX
PF   26-MAY-1998;   98WO-GB001514.
XX
PR   23-MAY-1997;   97GB-00010807.
XX
PA   (MEDI-) MEDICAL RES COUNCIL.
XX
PI   Choo Y,  Klug A,  Isalan M;
XX
DR   WPI; 1999-045308/04.
XX
PT   Preparation of nucleic acid binding proteins - by designing protein
PT   sequences of a Cys2-His2 zinc finger class based on a nucleic acid base
PT   triplet in a target nucleic acid sequence.
XX
PS   Example 4; Fig 5C; 62pp; English.
XX
CC   The present sequence represents finger 1 of a nucleic acid binding
CC   protein (NABP) specific for a G12V mutant ras oncogene. The specification
CC   describes a method for preparing a NABP of the Cys2-His2 zinc finger
CC   class capable of binding to a nucleic acid base triplet in a target
CC   nucleic acid sequence. Binding to the 5' base of the triplet by an alpha-
CC   helical zinc finger nucleic acid binding motif in the protein is
CC   determined as follows: (a) if the 5' base in the triplet is A, then
CC   position +6 in the alpha -helix is Glu, Asn or Val; (b) if the 5' base in
CC   the triplet is C, then position +6 in the alpha-helix is Ser, Thr, Val,
CC   Ala, Glu or Asn. The methods can be used for designing a protein which is
CC   capable of binding to any predefined nucleic acid sequence. The NABPs can
CC   be used for the detection of target nucleic acid molecules. They can also
CC   be used in gene therapy, e.g. for the delivery of functional genes into
CC   defective genes, or the delivery of nonsense nucleic acid to disrupt
CC   undesired nucleic acid
XX
SQ   Sequence 27 AA;

  Query Match             4.2%;  Score 7;  DB 2;  Length 27;
  Best Local Similarity   100.0%;  Pred. No. 12;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        109 HTRTHTG 115
              |||||||
Db         19 HTRTHTG 25
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